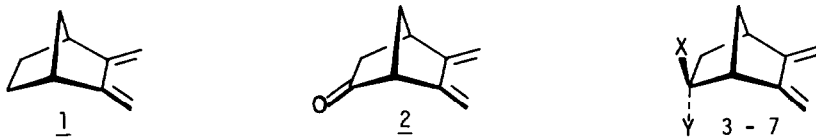


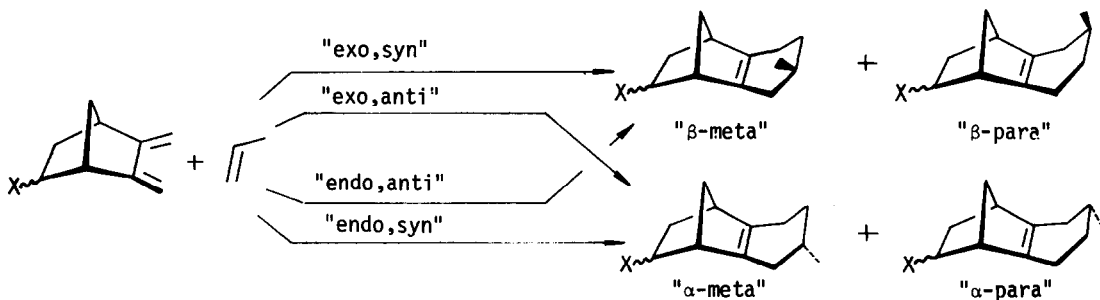
REGIOSELECTIVITY OF THE DIELS-ALDER CYCLOADDITIONS OF  
2-SUBSTITUTED 5,6-BIS(METHYLENE)-NORBORNANES.

Pierre-Alain Carrupt, Marco Avenati, Daniel Quarroz and Pierre Vogel\*  
Institut de chimie organique de l'Université, 2, rue de la Barre,  
CH 1005 Lausanne, Switzerland.

Chemical and spectroscopic properties of the *s*-cis butadiene function in 2,3-bis(methylene)-norbornane (1) can be modified without direct substitution of the diene moiety.<sup>1</sup> We have shown recently that the carbonyl group in 5,6-bis(methylene)-2-norbornanone (2) exerts a rate retardation effect on the Diels-Alder additions of this diene, relative to those of 1, that can be attributed to the transannular interaction between the homoconjugated butadiene and keto groups fixed in a rigid conformation.<sup>2</sup> This interaction was apparent from the comparison of the UV absorption<sup>2</sup> and <sup>13</sup>C-NMR spectra<sup>1b</sup> of 2 with those of 1.



The hydroxy groups in 5,6-bis(methylene)-exo-2-norbornanol (3) and in 5,6-bis(methylene)-exo-2,3-norbornanediol<sup>2</sup> were found to exert, however, a much smaller retardation effect on the cycloadditions of these dienes compared with 1 and 2. Since the 2-substituted 5,6-bis(methylene)-norbornanes can be prepared in optically pure forms<sup>3</sup>, they might become interesting



synthons if their cycloadditions were regioselective with acetylenic dienophiles and regio- and stereoselective with olefinic dienophiles.

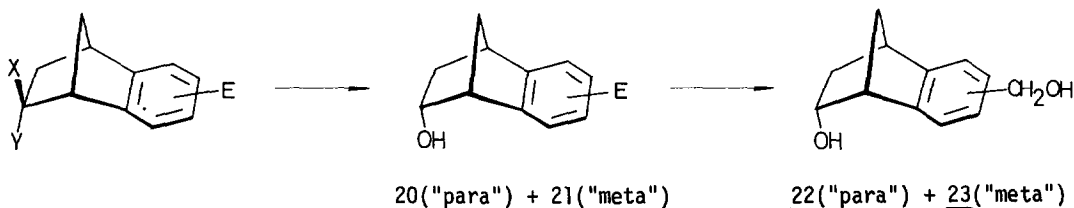
We wish to report our preliminary results on the regioselectivity of the Diels-Alder additions of 2 - 7 (see Table 1) to methyl propionate (MP). The highest regioselectivity was obtained with the dienes 2 & 7<sup>4</sup>; it is probably controlled by frontier and extra-frontier molecular orbitals (MO) of the addents.

The dienes 2 - 7 mixed with a 6 - 7 fold excess of degassed MP were heated to 80° in sealed tubes for 15 - 20 h.<sup>5</sup> After removal of the MP excess in vacuo, the adduct mixtures from 2 - 6 + MP were distilled (yield: 92 - 97 %) and analyzed by <sup>13</sup>C-NMR. The reaction mixture of 7 + MP was analyzed without purification. Our results are summarized in the Table 1.

Table 1: Regioselectivities of the Diels-Alder additions of methyl propionate to 2-substituted 5,6-bis(methylene)-norbornanes 2 - 7.

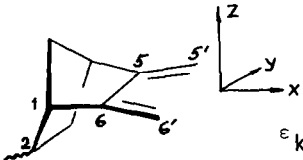
Diene	Adducts: "para"	"meta"
X, Y = 0 <u>2</u>	<u>8</u> : 80 - 75 %	<u>9</u> : 20 - 25 %
X = OH, Y = H <u>3</u>	<u>10</u> : 45 - 50 %	<u>11</u> : 55 - 50 %
X = OAc, Y = H <u>4</u>	<u>12</u> : 46 - 48 %	<u>13</u> : 54 - 52 %
X = H, Y = OH <u>5</u>	<u>14</u> : 28 - 36 %	<u>15</u> : 72 - 64 %
X = H, Y = OAc <u>6</u>	<u>16</u> : 70 - 65 %	<u>17</u> : 30 - 34 %
X = H, Y = OBs <u>7</u>	<u>18</u> : 82 - 80 %	<u>19</u> : 18 - 20 %

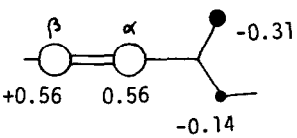
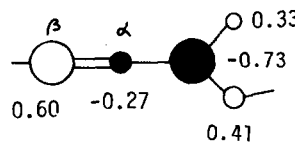
The structure of the regioisomers 8 - 19 were deduced from their <sup>13</sup>C-NMR characteristics and by derivatization into the corresponding endo-2-benzonorborn-5-enols 20 + 21 and 22 + 23<sup>6</sup> whose aromatic carbons could be recognized unambiguously in their proton coupled <sup>13</sup>C-NMR spectra (<sup>3</sup>J(CH) = 7 - 10 Hz<sup>7</sup>). The assignments were confirmed by the use of Yb(dpm)<sub>3</sub> applied to 8 - 19 and to corresponding aromatic derivatives obtained by oxidation with DDQ (2,3-dichloro-5,6-dicyanobenzoquinone) in benzene (20°, 20 h).



To a first approximation, geometry factors should not play a dominating role in determining the regioselectivity of the cycloadditions of 2 - 7 to MP because all our dienes are grafted onto rigid norbornane skeletons. Moreover, the dienes are differentiated by remote substitution only. If dipole-dipole interactions were responsible for the "para" regioselectivity observed with 2, 6 and 7, we do not understand why the same regioselectivity is not measured with 3 - 5. An exothermicity of 40 - 50 kcal/mol is estimated for the cycloadditions of 1 - 7 to an acetylenic dienophile. <sup>1a</sup> This fact together with the points outlined above make these reactions ideal cases for a rationalization based on perturbational MO theory. <sup>8</sup>

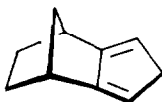
**Table 2:** Eigenvalues ( $\epsilon$ , eV) and  $2p_z$  coefficients ( $c_i$ ) at the olefinic carbons in the FMO's of dienes 1 - 6 and dienophile MP calculated by the EHT on MINDO/3 minimized geometries. <sup>9</sup>



	HOMO's					LUMO's				
	$\epsilon_k$	$c_i$ at C-5, C-5', C-6, C-6'				$\epsilon_{k+1}$	$c_i$ at C-5, C-5', C-6, C-6'			
diene <u>1</u>	-12.4	-0.31	-0.53	0.31	0.53	-8.9	0.5	-0.62	0.5	-0.62
<u>2</u>	-12.3	-0.23	-0.43	0.29	0.53	-9.1	-0.24	0.3	-0.3	0.4
<u>3</u>	-12.3	0.29	0.5	-0.31	-0.54	-8.9	-0.5	0.61	-0.49	0.61
<u>4</u>	-12.3	-0.29	-0.51	0.30	0.53	-9.0	-0.5	0.61	-0.49	0.61
<u>5</u>	-12.3	0.28	0.49	-0.30	-0.53	-8.9	-0.5	0.62	-0.5	0.61
<u>6</u>	-12.3	-0.3	-0.51	0.31	0.53	-8.9	-0.49	0.60	-0.49	0.61
dienophile MP	-13.5					-9.5				

According to this theory and to a first approximation <sup>8a</sup>, the shapes of the frontier molecular orbitals (FMO) of the dienes and dienophiles (cf. Table 2) should enable us to predict the regioselectivity of their cycloadditions. The coefficients ( $c_i$ ) of the HOMO of MP are the same at carbons  $C_\alpha$  and  $C_\beta$ ; moreover, the coefficients at the carboxylate centres are relatively small <sup>10</sup>. This indicates that the HOMO(MP)-LUMO(dienes) interactions should not be important in determining the regioselectivities. A dominating role is played probably by the LUMO(MP)-HOMO (dienes) interactions. Accordingly, one can predict (from the  $c_i$  reported in Table 2) that the ketodiene 2 must show the highest "para" regioselectivity (the highest overlap is realized between C-6' of 2 and  $C_\beta$  of MP), whereas the other dienes 3 - 6 should show a smaller "para" regioselectivity. Our results are in agreement with these predictions for MP + 2. The Diels-Alder additions of the exo-2-substituted derivatives 3 and 4 are not regioselective, in agreement with our FMO analysis (unsignificant "polarization" of the diene HOMO's) and with the observation that the polar exo-2-hydroxy group does not perturb significantly the reactivity of the 5,6-bis(methylene)-norbornanes. <sup>2</sup> The "meta" regioselectivity observed with the endo-2-

-hydroxy-diene 5 is unexpected. This suggests that simple FMO theory cannot be applied to that reaction (and probably others displaying relatively small regioselectivities); another gratuitous statement is to invoke the role played by secondary MO interactions. One can envision the dienophile attacking the diene preferentially on its endo face (because of favourable interactions between subjacent  $\pi$  and  $\sigma$ -type MO's of the diene and dienophile), as has been recently



24

reported for the cycloadditions of MP and methyl acrylate to the diene 24.<sup>11</sup> If this is true, the endo-2 substituents in 5 - 7 can perturb the cycloadditions: the bulk of the acetate in 6 or of the brosylate group in 7 would favor the "endo-para" additions, whereas the endo-2-hydroxy group in 5 would lead to "endo-meta" regioselectivity due to hydrogen bridging

with the ester group of MP. Work is under way to scrutinize these hypotheses.

#### References and Notes :

- 1) a) M. Hardy, P.A. Carrupt & P. Vogel, *Helv. chim. Acta* 59, 1685 (1976); P. Vogel, *Chimia* 31, 53 (1977); b) D. Quarroz, J.-M. Sonney, A. Chollet, A. Florey & P. Vogel, *Org. Magn. Reson.* 9, 611 (1977).
- 2) A. Chollet, C. Mahaim, C. Foetisch, M. Hardy & P. Vogel, *Helv. chim. Acta* 60, 59 (1977).
- 3) J.-M. Sonney, Dissertation, EPF-Lausanne, 1978.
- 4) The addition of methylvinylketone to 2 afforded only one major para-adduct (75 - 80%, by <sup>13</sup>C-NMR) thus demonstrating not only the regioselectivity of that cycloaddition but also its stereoselectivity. Para-regio + stereoselectivity was also observed with acrylic acid. The structures of the corresponding adducts are under investigation.
- 5) Dienes 1 - 7 are rapidly polymerized in the presence of traces of radicals, acids or air. The adducts 8 - 19 were found to aromatize easily by heating them in the presence of various impurities (acids, metals, air, etc.).
- 6) Details on these reactions will be given in a full paper.
- 7) M.J. Shapiro, *J. Org. Chemistry* 43, 212 (1978); E.B. Whipple, *Org. Magn. Reson.* 10, 23 (1977); V. Lucchini & P. R. Wells, *ibid.* 10, 112 (1977); H. Nery, D. Canet, B. Azoui, L. Lalloz & P. Caubère, *ibid.* 10, 240 (1977); H. Günther, H. Seel & M. E. Günther, *ibid.* 11, 97 (1978).
- 8) a) O. Eisenstein, J.M. Lefour, N.T. Anh & R.F. Hudson, *Tetrahedron* 33, 523 (1977); b) K.N. Houk, *Acc. Chem. Res.* 8, 361 (1975); V. Bachler & F. Mack, *Tetrahedron* 33, 2857 (1977); *Theoret. Chim. Acta* 43, 121 (1976); L.E. Overman, G.F. Taylor, K.N. Houk & L.N. Domelsmith, *J. Amer. Chem. Soc.* 100, 3182 (1978) and ref. cited therein.
- 9) Comparable coefficients were calculated for the FMO's of 1 - 6 and MP with the CNDO/2, MINDO/3 and EHT methods and they were insensitive to small changes of the geometries and other calculation parameters.
- 10) 1,3-interactions between the MO's of the cycloaddends reaching the geometries of the Diels-Alder transition states cannot be neglected a priori.
- 11) T. Sugimoto, Y. Kobuke & J. Furukawa, *J. Org. Chemistry* 41, 1457 (1976).

(Received in UK 2 August 1978)